PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/052388	30.09.2004	30.09.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/18, A61K31/426, A61K31/421, A61P31/14

Applicant
TIBOTEC PHARMACEUTICALS LTD.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/052388

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-16
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	15,16
Industrial applicability (IA)	Yes:	Claims	1-16
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: US-B1-6 514 953 (ARMITAGE IAN GORDON ET AL) 4 February 2003 (2003-02-04)

D2: WO 03/064416 A (GHIRO ELISE ;BAILEY MURRAY D (CA); LLINAS-BRUNET MONTSE (CA); BOEH) 7 August 2003 (2003-08-07)

D3: US 2003/050229 A1 (LACOLLA PAULO ET AL) 13 March 2003 (2003-03-13)

D4: JOHANSSON ANJA ET AL: "Acyl sulfonamides as potent protease inhibitors of the hepatitis C virus full-length NS3 (protease-helicase/NTPase): A comparative study of different C-terminals." BIOORGANIC AND MEDICINAL CHEMISTRY, vol. 11, no. 12, 12 June 2003 (2003-06-12), pages 2551-2568, XP002272318 ISSN: 0968-0896 (ISSN print)

D5: WO 95/06030 A (MUELLER RICHARD A ;VAZQUEZ MICHAEL L (US); MONSANTO CO (US); SEARL) 2 March 1995 (1995-03-02)

D6: DATABASE MEDLINE [Online] US NATIONAL LIBRARY OF MEDICINE (NLM), BETHESDA, MD, US; 1 April 2002 (2002-04-01), PALMON RON ET AL: "Lack of hepatotoxicity associated with nonnucleoside reverse transcriptase inhibitors." XP002319202 Database accession no. NLM11917237

D7: WO 03/053435 A (TIBOTEC PHARMACEUTICALS LTD; VENDEVILLE, SANDRINE, MARIE, HELENE; VERS) 3 July 2003 (2003-07-03)

For what concerns the most relevant paragraphs of the above-mentioned documents, please see citations in the International Search Report, unless otherwise indicated.

1. NOVELTY

The present application seems to meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-14 appears to be new over the available prior art in the sense of Article 33(2) PCT.

As a matter if fact, none of the available documents (D1-D7) discloses the use of a class of compounds which fall into the general formula given in claim 1 for the manufacture of a medicament suitable for the treatment of HCV.

2. INVENTIVE STEP

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 15 and 16 does not involve an inventive step in the sense of Article 33(3) PCT.

Claims 15 and 16 are directed to a **composition** which comprises a sulfonamide falling in the general formula given in claim 1 together with another anti-HCV agent (claim 15) and anti-HIV agent (claim 16).

The document D7 is regarded as being the closest prior art to the subject-matter of claim 15 and discloses molecules falling into the formula claimed in claim 1 for the treatment of HIV and other viral infections.
Moreover, D7 discloses the use of a combination comprising a) a compound falling in the genera formula given in claim 1 of the present application and b) another antiviral compound (see for example the list on page 31, 2nd par.)

The subject-matter of claim 15 therefore differs from this known D7 in that the additional compound to the one claim is indicated as anti-HCV agent.

The problem to be solved by the present invention may therefore be regarded as the provision of a combination of two compounds with the same anti-HCV activity.

The solution proposed in claim 15 of the present application cannot be considered as involving an inventive step (Article 33(3) PCT).
As a matter of fact, D6 already discloses the use of delavirdine, efavirenz or nevirapine (which are mentioned in D7 as additional compounds to the one claimed) for the treatment of HIV patients co-infected with HCV.

The same reasoning applies, mutatis mutandis, to the subject-matter of the corresponding

independent claim 16 which therefore is also considered not inventive.